Not for Publication

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

ANDREW NELSON, *Plaintiff,* v. BIOGEN IDEC, INC. and ELAN PHARMACEUTICALS, LLC, *Defendants.*	Civil Action No. 12-7317 (JMV) (MF) **OPINON**

John Michael Vazquez, U.S.D.J.

This matter is a prescription drug product liability action. Currently pending before the Court are two motions by Defendants Biogen Idec, Inc., and Elan Pharmaceuticals, LLC: one for summary judgment, D.E. 154, and one to exclude expert testimony, D.E. 155.[1] The product at issue is Defendants' multiple sclerosis drug, Tysabri. After taking Tysabri, Plaintiff Andrew Nelson contracted progressive multifocal leukoencephalopathy ("PML"), a dreadful and potentially fatal brain disease caused by the JC Virus. Plaintiff sued Defendants under the New Jersey Product Liability Act for failure to adequately warn of the risks of Tysabri. The Court reviewed the submissions made in support of and in opposition to the motion and considered the motion without oral argument pursuant to Fed. R. Civ. P. 78(b) and L. Civ. R. 78.1(b). Three other

[1] Defendants' Memorandum of Law in Support of Defendants' Joint Motion for Summary Judgment, D.E. 154-1, hereinafter "Defendants' Brief" or "Def. Br."; Plaintiff's Opposition to Defendants' Joint Motion for Summary Judgment, D.E. 158, hereinafter "Opposition" or "Opp."; Reply Brief in Support of Defendants' Joint Motion For Summary Judgment and Joint Motion to Preclude the Expert Testimony of Eugene O. Major, Ph.D., D.E. 160; hereinafter "Reply Brief" or "Reply Br."

trial courts, two federal and one state, have considered the same allegations against the same Defendants, albeit pursuant to the laws of other states. Defendants have prevailed at the summary judgment stage in all three cases. For the reasons that follow, Defendants also prevail here. Defendants' motion for summary judgment is **GRANTED** and their *Daubert* motion is **DENIED** as moot.

I. Factual Background & Procedural History[2]

Defendants Biogen Idec, Inc. ("Biogen") and Elan Pharmaceuticals, LLC ("Elan") collaborated on the research, development, and marketing of the multiple sclerosis ("MS") drug natalizumab, which is sold under the brand name Tysabri. Defendants' SOMF at ¶5. Tysabri is a humanized monoclonal antibody that protects against demyelination in those suffering from MS. Biogen is the manufacturer of the drug and holds the FDA license for it. *Id.* Elan distributed Tysabri in the United States and also marketed it as a treatment for Crohn's disease. *Id.*

The Food and Drug Administration ("FDA") approved Tysabri for treatment of relapsing-remitting MS in 2004. *Id.* at ¶27. In 2005, Defendants withdrew Tysabri from the market and suspended clinical trials after two patients developed PML. *Id.* at ¶¶29, 34. The JC Virus causes PML. *Id.*at ¶31. Until 2010, according to Defendants, it was "generally accepted in the scientific community that upwards of 80% of adults had been exposed to the JC Virus[.]" *Id.* at ¶33. Plaintiff disputes that the number is "generally accepted," claiming that sources differ and that the percentage has been reported as low as 35% and as high as 90%. Plaintiff's SOMF at ¶33.

In 2006, the FDA requested that Biogen test patients for the presence of the JC Virus antibody before the patients were entered into additional Tysabri clinical trials. Defendants'

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[2] The facts are taken from the parties' respective statements of material fact: Defendants' Statement of Material Facts Not in Dispute, D.E. 154-2 ("Defendants' SOMF"), and Plaintiff's Statement of Material Facts in opposition, D.E. 159 "(Plaintiff's SOMF").

SOMF at ¶37. Later that year, Biogen submitted a report to the FDA stating that testing performed at the National Institute of Health ("NIH") did not provide a "clinically relevant cut off" for detecting the JC Virus antibody. *Id.* at ¶38. The NIH testing was led by Plaintiff's expert, Dr. Eugene Major, Ph.D. *Id.* The FDA convened an Advisory Panel to consider permitting Tysabri back on the market on March 7 and 8, 2006. *Id.* at ¶39.

On June 5, 2006, the FDA re-approved Tysabri with a number of new labelling requirements regarding the PML risk, including a "black box" warning. *Id.* at ¶41. A "boxed" or a "black box" warning is the "strongest warning required or permitted by the FDA," and is used to indicate that there is a serious risk associated with use of the drug. *Id.* at ¶¶12-13. As of April 2008, the warning read:

> WARNING: PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY
>
> TYSABRI® increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. Although the cases of PML were limited to patients with recent or concomitant exposure to immunomodulators or immunosuppressants, there were too few cases to rule out the possibility that PML may occur with TYSABRI monotherapy [see Warnings and Precautions (5.1)].
>
> - Because of the risk of PML, TYSABRI is available only through a special restricted distribution program called the TOUCH™ Prescribing Program. Under the TOUCH™ Prescribing Program, only prescribers, infusion centers, and pharmacies associated with infusion centers registered with the program are able to prescribe, distribute, or infuse the product. In addition, TYSABRI must be administered only to patients who are enrolled in and met all the conditions of the TOUCH™ Prescribing Program [see Warnings and Precautions (5.1, 5.2)].
>
> - Healthcare professionals should monitor patients on TYSABRI for any new sign or symptom that may be suggestive of PML. TYSABRI dosing should be

> withheld immediately at the first sign or symptom suggestive of PML. For diagnosis, an evaluation that includes a gadolinium-enhanced magnetic resonance imaging (MRI) scan of the brain and, when indicated, cerebrospinal fluid analysis for JC viral DNA are recommended [*see Contraindications (4), Warnings and Precautions (5.1)*.].[3]

Defendants' SOMF at ¶14.

The FDA also required that a Tysabri medication guide be provided to physicians and infusion nurses who would be administering the medication. *Id.* at ¶47. As noted in the warning, the FDA permitted Tysabri to be prescribed through the Tysabri Outreach: Unified Commitment to Health ("TOUCH") program, an FDA-mandated "Risk Evaluation and Management Strategy," or "REMS," program. *Id.* at ¶48. As part of the TOUCH program, the medication guide was provided directly to patients. *Id.* The TOUCH program also required doctors prescribing Tysabri to acknowledge the risk of PML as well as get written consent from the patient concerning the risks. *Id.* at ¶53. The patient also had to confirm that he had read the medication guide before each infusion as well as answer a series of questions about the risk of PML. *Id.* at ¶54-55. The nurse administering the infusion also screened the patient for any warning signs of PML. *Id.*

In the prescribing information, the PML risk was described as follows:

> Progressive multifocal leukoencephalopathy, an opportunistic infection caused by the JC virus that typically occurs in patients that are immunocompromised, has occurred in 3 patients who received TYSABRI® in clinical trials (see BOXED WARNING). Two cases

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[3] This paragraph was changed in July 2010 to read:

> TYSABRI® increases the risk of progressive multifocal leukoencephalopathy (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability. Cases of PML have been reported in patients taking TYSABRI who were recently or concomitantly treated with immunomodulators or immunosuppressants, as well as in patients receiving TYSABRI as monotherapy [*see Warnings and Precautions (5.1)*].

Defendants' SOMF at n. 1.

> of PML were observed in 1869 patients with multiple sclerosis treated for a median of 120 weeks. The third case occurred among 1043 patients with Crohn's disease after the patient received 8 doses. The absolute risk for PML in patients treated with TYSABRI® cannot be precisely estimated, and factors that might increase an individual patient's risk for PML have not been identified. There are no known interventions that can reliably prevent PML or adequately treat PML if it occurs. It is not known whether early detection of PML and discontinuation of TYSABRI® will mitigate the disease. There is limited experience beyond 2 years of treatment. The relationship between the risk of PML and the duration of treatment is unknown.
>
> All three cases of PML occurred in patients who were concomitantly exposed to immunomodulators (interferon beta in the patients with multiple sclerosis) or were immunocompromised due to recent treatment with immunosuppressants (e.g., azathioprine in the patient with Crohn's disease). Ordinarily, therefore, patients receiving chronic immunosuppressant or immunomodulatory therapy or who have systemic medical conditions resulting in significantly compromised immune system function should not be treated with TYSABRI®. However, the number of cases is too few and the number of patients treated too small to reliably conclude that the risk of PML is lower in patients treated with TYSABRI® alone than in patients who are receiving other drugs that decrease immune function or who are otherwise immunocompromised.

Id. at ¶45. The prescribing information also stated that

> (PML), an opportunistic viral infection of the brain that usually leads to death or severe disability (**see BOXED WARNING AND WARNINGS, Progressive Multifocal Leukoencephalopathy**), TYSABRI® is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, alternate multiple sclerosis therapies.

Id. at ¶46 (emphasis in original).

While Plaintiff was receiving Tysabri infusions through the TOUCH program, the medication guide provided the following:

> **What is the most important information I should know about TYSABRI®?**

- **TYSABRI® increases your chance of getting a rare brain infection that usually causes death or severe disability. This infection is called progressive multifocal leukoencephalopathy (PML).** PML usually happens in people with weakened immune systems.
    - No one can predict who will get PML.
    - There is no known treatment, prevention, or cure for PML.

Id. at ¶49 (emphasis in original). The TOUCH program acknowledgement also required patients to sign and initial a form that contained the following acknowledgement:

> I acknowledge that . . . TYSABRI increases your change of getting a rare brain infection that usually causes death or severe disability.
> - This infection is called progressive multifocal leukoencephalopathy (PML). PML usually happens in people with weakened immune systems
> - No one can predict who will get PML There is no known treatment, prevention, or cure for PML

Id. at ¶15.

In August 2008, the FDA approved an addition to the Tysabri label "stating that Tysabri associated PML can occur in cases of Tysabri monotherapy." *Id.* at ¶103. Two more cases of Tysabri-associated PML were reported in 2008. *Id.* at ¶104. By July 24, 2009, eleven cases had been reported. *Id.* at ¶105. In November 2009, the label was updated to read: "In patients treated with Tysabri, the risk of PML increase [sic] with longer treatment duration . . . ." *Id.* at ¶107. In July 2010, another update was added, stating: "The risk of PML is also increased in patients who have been treated with an immunosuppressant prior to receiving Tysabri . . . ." *Id.* at ¶108.

In 2006, Biogen was using the ELISA assay to detect JC Virus antibodies in patients who participated in Tysabri clinical trials. *Id.* at ¶38. On March 2, 2006, Biogen submitted data from a National Institute of Health ("NIH") test—performed at a lab run by Plaintiff's proffered expert—whose report "concluded '[c]urrently there is no consensus on a clinically relevant cut off for the ELISA assay or JCV antibody detection.'" *Id.* From 2006 through 2010, Defendants

developed a different assay, the Polymerase Chain Reaction ("PCR") assay, which was "thought to be the most likely risk stratification tool" to identify those with the JC Virus. *Id.* at ¶112. However, in 2010, the *Annals of Neurology* indicated that PCR testing was "unlikely to be useful" to test Tysabri patients. *Id.* at ¶113.

In 2009, Biogen convened an advisory board of "MS experts and regulatory experts" to discuss Biogen's JC Virus antibody assay. As of December 2009, the board concluded that the "data on the assay was too preliminary to be of predictive value" as to PML. *Id.* at ¶¶127-29. On September 8, 2010, Defendants met with the FDA's Center for Drug Evaluation and Research ("CDER") to propose "a potential labelling change" based on Biogen's JC Virus antibody assay and research. The FDA rejected the proposal, in part because "only [seventeen] patients had pre-PML antibody status tested." *Id.* at ¶¶131-33. Two months later, on November 18, 2010, Defendants met with the FDA Center for Devices and Radiological Health ("CDRH") with a Biogen proposal to provide their JC Virus antibody assay to Tysabri prescribers. The FDA also rejected this proposal as the "usefulness" of the assay "ha[d] not been established." *Id.* at ¶¶134-35.

Over the next year, Biogen sponsored two clinical trials, STRATIFY-1 and STRATIFY-2, to study blood samples of MS patients using Tysabri. *Id.* at ¶138. Biogen requested another labelling change in October 2011 in light of the ongoing trials, which included data on thirty-seven Tysabri patients. *Id.* at ¶140. On January 20, 2012, the FDA cleared the STRATIFY JC Virus antibody assay and approved a labelling change "regarding the significance of JCV antibodies." *Id.* at 141. In its announcement, the FDA stated that Biogen's test was "the first [] for risk of rare brain infection in some people treated with Tysabri." *Id.*

Plaintiff was diagnosed with MS in October 2002. *Id.* at ¶6. He was prescribed Tysabri

by Dr. Jana Preiningerova in April 2008 and had his first infusion in May 2008. *Id.* at ¶¶7- 8. Before starting the infusions, Dr. Preiningerova discussed the risk of PML with Plaintiff. *Id.* at ¶66. When Dr. Preiningerova prescribed Tysabri, the label stated that "the relationship between the risk of PML and the duration of treatment is unknown." *Id.* at ¶100. After he moved, Plaintiff continued using Tysabri with Dr. Rana Zabad, and then with Dr. Kenneth Citak. *Id.* at ¶¶9-10. Like Dr. Preiningerova, Dr. Zabad discussed the risks of Tysabri with Plaintiff. *Id.* at ¶72. Dr. Zabad also tested Plaintiff for the JC Virus in 2009, and the result was negative. *Id.* at ¶74. Plaintiff continued receiving Tysabri treatments through September 2010, when he began showing signs of PML. *Id.* at ¶14. In November 2010, Plaintiff's cerebrospinal fluid was tested for the JC Virus, but none was found. *Id.* at ¶79. In December 2010, Plaintiff had a brain biopsy which "found evidence of PML[,]" and Plaintiff was diagnosed with PML. *Id.* at ¶79.

Plaintiff filed his Complaint on November 28, 2012. D.E. 1. He then filed an Amended Complaint on January 2, 2013. D.E. 4. In response, Biogen and Elan filed motions to dismiss. D.E. 8, 21. Judge Linares granted in part and denied in part the motions, allowing Plaintiff to file a Second Amended Complaint but dismissing Plaintiff's claim for punitive damages with prejudice. D.E. 34. Plaintiff filed a motion for reconsideration as well as a Second Amended Complaint. D.E. 35, 37. The Court denied the motion for reconsideration. D.E. 44. Both Defendants filed a motion to dismiss Count One of the Second Amended Complaint and the demand for punitive or multiple damages on July 19, 2013. D.E. 48. The motion was granted, and the Court ordered Plaintiff to withdraw Court One and his requests for treble and/or punitive damages. D.E. 51. Plaintiff then filed his Third Amended Complaint on September 20, 2013. D.E. 52.

The case was transferred to the undersigned on February 25, 2015. D.E. 129. After

discovery began in earnest, the Court granted Plaintiff's motion to file a Fourth Amended Complaint, which was filed on June 13, 2016. D.E. 121, 141, 142. Defendants filed a motion to set aside the Court's decision to allow Plaintiff to file a Fourth Amended Complaint, or in the alternative, to dismiss Count Two, for negligent undertaking. D.E. 144. The Court denied the motion to set aside but granted the motion as to Count Two, dismissing it with prejudice. D.E. 150, 151. As a result, only one count remains against both Defendants for violations of the New Jersey Products Liability Act ("NJPLA"), N.J.S.A. 2A:58C-2. Plaintiff's count is premised on a failure to warn.

Defendants filed the instant motions on May 15, 2017: one for summary judgment, D.E. 154, and one to preclude the expert testimony of Eugene O. Major, Ph.D. D.E. 154, 155. Plaintiff filed opposition, D.E. 157, 158, to which Defendants have replied. D.E. 160.

II. Standard of Review

Summary judgment is proper where the moving party "shows that there is no genuine dispute as to any material fact," and the moving party is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(a); *Abraham v. Raso*, 183 F.3d 279, 287 (3d Cir. 1999). A fact in dispute is material when it "might affect the outcome of the suit under the governing law" and is genuine "if the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986). Disputes over irrelevant or unnecessary facts will not preclude granting a motion for summary judgment. *Id.* "In considering a motion for summary judgment, a district court may not make credibility determinations or engage in any weighing of the evidence; instead, the nonmoving party's evidence 'is to be believed and all justifiable inferences are to be drawn in his favor.'" *Marino v. Indus. Crating Co.*, 358 F.3d 241, 247 (3d Cir. 2004) (quoting *Anderson*, 477 U.S. at 255)). A court's role in deciding a motion

for summary judgment is not to evaluate the evidence and decide the truth of the matter but rather "to determine whether there is a genuine issue for trial." *Anderson*, 477 U.S. at 249.

A party moving for summary judgment has the initial burden of showing the basis for its motion and must demonstrate that there is an absence of a genuine issue of material fact. *Celotex Corp. v. Catrett*, 477 U.S. 317, 323 (1986). After the moving party adequately supports its motion, the burden shifts to the nonmoving party to "go beyond the pleadings and by her own affidavits, or by the depositions, answers to interrogatories, and admissions on file, designate specific facts showing that there is a genuine issue for trial." *Id.* at 324 (internal quotation marks omitted). To withstand a properly supported motion for summary judgment, the nonmoving party must identify specific facts and affirmative evidence that contradict the moving party. *Anderson*, 477 U.S. at 250. "[I]f the non-movant's evidence is merely 'colorable' or is 'not significantly probative,' the court may grant summary judgment." *Messa v. Omaha Prop. & Cas. Ins. Co.*, 122 F. Supp. 2d 523, 528 (D.N.J. 2000) (quoting *Anderson*, 477 U.S. at 249-50)).

Ultimately, there is "no genuine issue as to any material fact" if a party "fails to make a showing sufficient to establish the existence of an element essential to that party's case." *Celotex Corp.*, 477 U.S. at 322. "If reasonable minds could differ as to the import of the evidence," however, summary judgment is not appropriate. *See Anderson*, 477 U.S. at 250-51.

III. Analysis

At the outset, neither party disputes that New Jersey law applies. Def. Br. at 18, Opp. at 10. In their motion for summary judgment, Defendants make several arguments. Defendants argue that the Tysabri label is entitled to a "super-presumption" of adequacy under the NJPLA because it was FDA-approved. Def. Br. at 19-20. They also assert that Plaintiff was adequately informed of the risk of PML by his prescribing doctors. *Id.* at 22. Defendants further indicate that

Plaintiff lacks necessary expert testimony regarding the adequacy of the label. *Id.* at 23-26. Defendants add that Plaintiff cannot prove proximate cause. *Id.* at 28-31. In addition, Defendants state that Plaintiff's NJPLA claim is preempted by federal law. *Id.* at 31-37. Finally, Elan argues that it could not have sought a change in the labeling because it is not the license holder for Tysabri, and, as a result, it is entitled to summary judgment. *Id.* at 39-40.

Plaintiff responds that there are genuine issues of material fact which preclude summary judgment. Plaintiff argues that, at this stage, the evidence sufficiently rebuts the presumption that the label was adequate. Opp. at 10-17. He also asserts that Dr. Major's testimony appropriately addresses the adequacy of the Tysabri label. Plaintiff continues that there is a genuine issue of material fact as to whether he would have continued his course of treatment with Tysabri had the label been different. *Id.* at 17-28. Plaintiff further argues that Defendants' preemption argument fails because Defendants could have changed the label without FDA approval and that Elan cannot avoid liability even though it did not hold the license to Tysabri. *Id.* at 29-44.

a. *Amos, Christison, & Gentile*

Three courts in other jurisdictions have addressed the adequacy of the Tysabri label as it relates to PML: *Amos v. Biogen IDEC Inc. and Elan Pharmaceuticals, Inc.*, 249 F.Supp.3d 690 (W.D.N.Y. 2017); *Christison v. Biogen Idec. Inc. and Elan Pharmaceuticals, LLC*, 199 F.Supp.3d 1315 (D. Utah 2016); *Gentile v. Biogen Idec, Inc., et al*, 2016 Mass. Super. LEXIS 238 (Mass. Super. Ct. Feb. 14, 2014). The cases involved different plaintiffs, but the facts and legal issues were very similar to the case at bar, and the defendants in all three were Biogen and Elan. In addition, Dr. Major was the plaintiff's expert in each case. All three cases were decided in favor of Defendants. None of the decisions are binding on this Court because they were not decided by the Third Circuit or the United States Supreme Court. However, they can be considered persuasive

authority to the extent the relevant law of each jurisdiction is consistent with the NJPLA.

i. Gentile

The plaintiff in *Gentile* received Tysabri infusions from January 2007 to September 2009. *Gentile*, 2016 Mass. Super. LEXIS at *8. She was diagnosed with PML in October 2009 and died two months later. *Id.* Her husband brought a case against Biogen and Elan in Massachusetts, alleging a number of claims including failure to warn under New York law.

The court in *Gentile* dismissed the failure to warn claim, writing that the duty to warn of potential dangers

> did not impose on defendants an obligation to research and develop technologies to address the consequences or risks of taking the drug. The relevant question is whether Tysabri's warnings were adequate to warn a physician of the precise malady [plaintiff] developed . . . . "[W]hen a plaintiff claims to be injured in a manner that is addressed by warnings provided to his physician, summary judgment is granted on failure to warn claims."

Id. at *14-15 (internal citations omitted).

Although the matter was brought in Massachusetts, New York law applied. *Id.* at *12-13. New York, adheres to the "learned intermediary" rule: "the warnings about a prescription drugs 'are intended for the physician, whose duty it is to balance the risks against the benefits of various drugs.'" *Id.* at *14 (internal citations omitted). The *Gentile* court held that the Tysabri label in the years Mrs. Gentile received the medication, from January 2007 to September 2009, was adequate as a matter of law because it "warned against the precise risk (developing PML)" and "fully disclosed the serious consequences of the disease." *Id.* at *16.

Despite its determination that the warning was adequate, the court also found that plaintiff's claim failed for lack of expert testimony "[b]ecause the adequacy of the warnings cannot be evaluated by a layperson." *Id.* at *18. The court acknowledged that, "if accepted as true, [Dr.

Major's testimony] establishes that defendants did not efficiently investigate risk factors that could have been revealed sooner" as to the risk of developing PML. However, because Dr. Major admitted during his deposition that he is not familiar with prescription drug labeling, and is not a medical doctor who prescribes medication to patients, the *Gentile* court ruled his opinion inadmissible. *Id.* at *19-20.

The court in *Gentile* also granted defendants summary judgment on the ground that plaintiff could not demonstrate that the alleged inadequate warning was the cause of the harm, *i.e.* plaintiff could not show proximate cause. *Id.* at *20-23. The court reasoned that "[t]he unavailability of technology . . . does not fall within a failure to warn claim, which evaluates whether the information provided was sufficient to caution against the injury at issue." *Id.* at *22. In addition, the *Gentile* court noted that the prescribing physician testified that "she [plaintiff's doctor] was aware that Tysabri" increased the risk of PML. *Id.* at *16-17. The plaintiff argued that the three risk factors (JC Virus antibodies, duration of treatment, and prior immunosuppressant exposure) should have been included on the label, but the court held that even without these specific warnings, the label "when read as a whole," "unmistakably conveyed the seriousness of PML." *Id.* The court in *Gentile* added that plaintiff's prescribing doctor indicated that she would have prescribed Tysabri even if she had been informed of the additional warnings. *Id.* at *21.

The court in *Gentile* further ruled that defendants had no duty to warn the plaintiff directly under the learned intermediary rule. *Id.* at *23. Thus, the negligent undertaking claim was dismissed. *Id.* at *24. The court also found that plaintiff's failure to warn claims against both Biogen and Elan were preempted because the FDA did not allow Biogen to revise the label to include the JC Virus risk, and Elan could not have requested such a change. *Id.* at *25-28. In response to plaintiff's argument that defendants could have developed the JC Virus antibody assay

sooner, the court noted that rather than acquiescing to the FDA, defendants "continued to research the JCV antibody correlation until the FDA finally approved the modified warning." *Id.* at 27.

ii. Christison

In *Christison*, Mrs. Christison received infusions of Tysabri from February 2007 to June 2009. *Christison*, 199 F.Supp.3d 1315, at 1330-31. She was diagnosed with PML in July 2009 and died the next month. *Id.* at 1330. Her husband brought claims of negligence, negligent failure to warn, and negligent misrepresentation against Biogen and Elan in federal court in Utah. *Id.* at 1319. The *Christison* court granted summary judgment to defendants on all counts. *Id.* at 1318. Utah also used the "learned intermediary" rule. *Id.* at 1319-20.

The court in *Christison* described the two relevant assays that defendants attempted to develop: the PCR assay and the JC Virus antibody assay. *Id.* at 1334-5. After Tysabri was taken off the market in 2005, "Defendants' scientists and others in the field pursued what they thought to be the most likely risk stratification tool by devoting research efforts to finding JC virus in the blood and periphery through [PCR] assay testing." *Id.* at 1334. However, in 2010, the *Christison* court noted, the *Annals of Neurology* published data demonstrating that the PCR assay was "unlikely to be useful" as a PML risk stratification tool. *Id.* By 2009, Biogen scientists developed the JC Virus antibody assay, which was analytically, but not clinically, validated - meaning that it accurately showed the relevant markers of the virus but did not identify those patients "at increased risk for a serious adverse effect." *Id.* Even after Mrs. Christison passed away, regulators stated that the JC Virus antibody assay was "too preliminary to be of predictive value" as to PML. *Id.* at 1334.

The *Christison* court initially found that plaintiffs'[4] case failed because they did not present

[4] There were technically two plaintiffs in *Christison* because Mr. Christison sued on his own

expert testimony as to the "alleged inadequacies" of the Tysabri label, and thus could not show causation. *Id.* at 1340-42. The plaintiffs had argued that a jury was capable of analyzing the label themselves; the *Christison* court disagreed. *Id.* Rather, the court explained: "[The case] requires an expert who is familiar with drug labeling and the process by which a drug is prescribed to a patient." *Id.* at 1342. Plaintiffs' expert, Dr. Major, was not familiar with either area. *Id.* at 1339.

The *Christison* court also held that regardless of the lack of expert testimony, the Tysabri label in 2007 through 2009 was adequate as a matter of law. *Id.* at 1346. The court explained that given the black box warning as mandated by the FDA, along with the prescribing physician's testimony that the warning was adequate, the label "clearly convey[ed] a warning that taking Tysabri would increase the risk of PML." *Id.* at 1345. Because the warnings were adequate as a matter of law, the remaining state law claims failed. *Id.*[5]

The *Christison* court further found that plaintiffs' claims were preempted by federal law because, before 2012, it was clear the FDA would not have approved a label change. *Id.* at 1346-48. The court in *Christison* noted that a manufacturer generally must seek FDA approval to change a drug label that has already been approved but that manufacturers can add or strengthen a label without prior approval under the "changes being effected" or "CBE" exception. *Id.* at 1347. However, the court continued, if the manufacturer can show clear evidence that the FDA would

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behalf and on behalf of his wife's estate.

[5] The *Christison* court denied Biogen and Elan summary judgment as to the argument that they did not have a legal duty to develop an assay. *Id.* at 1345-46. The court found that the standard for reviewing defendants' duty is not whether they "had an obligation to engage in a *specific act*, such as developing an assay," but rather whether they "engaged in 'reasonable conduct in light of the apparent risk.'" *Id.* at 1346 (emphasis in original). The court did note that Dr. Major's testimony was admissible on the issue of "the state of technology and research" on the assay. *Id.* Even though Biogen and Elan were denied summary judgment on this ground, the court in *Christison* nevertheless dismissed the plaintiffs' entire case on other grounds.

not have approved the change, the CBE exception does not apply. *Id.* at 1346-47. The *Christison* court found clear evidence existed from CDER and CDRH's rejection of Biogen's requests in 2010. *See id.* (citing *In re Depakote*, 87 F.Supp.3d 916 (S.D. Ill., 2015); *Rheinfrank v. Abbott Labs*, 119 F.Supp.3d 749 (S.D. Ohio 2015)).

iii. Amos

Mrs. Amos took Tysabri from September 2006 to June 2011. *See Amos*, 249 F.Supp. 3d at 696. After being diagnosed with PML in July 2011, she died in September of that year. *Id.* at 693. Her husband sued Biogen and Elan on behalf of Mrs. Amos' estate, alleging inadequate warnings as to the risk of PML. *Id.*

As in *Gentile* and *Christison*, the learned intermediary rule applied in *Amos*. The court dismissed the failure to warn claims, finding that the warnings were "adequate as a matter of law." *Id.* at 697-698. The *Amos* court held that, read as a whole, "the warnings for Tysabri clearly, directly, and unequivocally informed treating physicians of the increased risk for PML." *Id.* at 698. The warnings were "the strongest . . . available" and described the "precise malady incurred." *Id.* at 697-698 (internal citations omitted).

The court in *Amos* also found that the failure to warn claims were preempted because defendants could not have changed the label without FDA approval, and the evidence demonstrated that FDA would not have approve the proposed change before 2012. *Id.* at 699. In support, the court cited to the "two 'smoking gun' rejections from the FDA", in September and November 2010. *Id.* at 699-700. The court in *Amos* additionally found that any state claim as to Elan was preempted because it could not have changed the Tysabri label under any circumstances because it was not the drug's license holder. *Id.* at 700.

b. The New Jersey Products Liability Act

The NJPLA provides:

> A manufacturer or seller of a product shall be liable in a product liability action only if the claimant proves by a preponderance of the evidence that the product causing the harm was not reasonably fit, suitable or safe for its intended purpose because it: a. deviated from the design specifications, formulae, or performance standards of the manufacturer or from otherwise identical units manufactured to the same manufacturing specifications or formulae, or b. failed to contain adequate warnings or instructions, or c. was designed in a defective manner.

N.J.S.A. 2A:58C-2.

As noted, the current matter concerns the adequacy of Tysabri's warning. In such cases, "the defect is in the failure to warn unsuspecting users that the product can potentially cause injury." *Zaza v. Marquess and Nell, Inc.*, 144 N.J. 34, 58 (1996). Under the NJPLA, a legally "adequate warning is one that a reasonably prudent person in the same or similar circumstances would have provided." *Id.* The "label does not have to have the best possible warning, but it must be sufficient to adequately convey the nature, extent, and seriousness of the risk in a clear unambiguous way to the prescribers of the drug." *In re Accutane Litigation*, 2017 WL 3138003, at *18 (App. Div. July 25, 2017). As to prescription medications, New Jersey also uses the "learned intermediary" rule. This means that the duty to warn is owed to the prescribing physician rather than the patient. *See Neimiera by Neimeira v. Schneider*, 114 N.J. 550, 552 (1989); *see also Seavey v. Globus Med. Inc.*, 2014 U.S. Dist. LEXIS 65985, at *32 (D.N.J. Mar. 11, 2014) ("When the learned intermediary doctrine applies, a drug or medical device manufacturer fulfills its duty to warn . . . when it provides a physician with an adequate warning about any dangerous propensities that product may have."); *Banner v. Hoffman-La Roche Inc.*, 891 A.2d 1229, 1236 (App. Div. 2006).

Under the NJPLA, a pharmaceutical warning is presumed to be adequate as a matter of law

if it is FDA-approved. N.J.S.A. 2A:58C-4; *Perez v. Wyeth Laboratories Inc.*, 161 N.J. 1, 24 (1999). The New Jersey Supreme Court has ruled that the presumption can be overcome in two instances: "For all practical purposes, absent deliberate concealment or nondisclosure of after-acquired knowledge of harmful effects, compliance with FDA standards should be virtually dispositive of such [failure to warn] claims." *Perez*, 161 N.J. at 25. The Supreme Court has further described the presumption as a "super-presumption," that can be rebutted only in "rare" cases. *Kendall v. Hoffman-La Roche, Inc.*, 209 N.J. 173, 197 (2012).

Here, Plaintiff fails to point to a genuine issue of material fact that will overcome the presumption of adequacy afforded by the NJPLA. Before Plaintiff began using Tysabri, the drug carried a "black box" warning, the strongest possible warning required or permitted by the FDA. The label specifically warned of the precise malady, PML, from which Plaintiff now suffers and indicated that Tysabri increases the risk of PML. The label clearly stated the dire consequences of PML, noting that the disease "usually leads to death or severe disability[.]" The label was also written clearly and required the additional safeguard of the TOUCH program. The TOUCH program ensured that only qualified physicians who are aware of the risks associated with Tysabri could administer it. The program likewise required that the patients themselves be regularly informed of the risk. In doing so, patients acknowledged not only the risks of PML but also that there is no known cure for the disease. As noted, the learned intermediary doctrine applies here, as it did in *Gentile*, *Christison*, and *Amos*. The Court agrees that, as matter of law, the label before Plaintiff began treatment was adequate as a matter of law concerning the prescribing physicians. In fact, the Tysabri warnings went beyond the norm of advising only the learned intermediary; the TOUCH program required direct warnings to the patient, including Plaintiff.

Plaintiff attempts to distinguish *Gentile*, *Christison*, and *Amos* by claiming that New Jersey

law contains a different standard. Specifically, Plaintiff argues that the reasonableness of the warning must be viewed through the lens of the warning's *sender*, not its *recipient*, *see* Opposition at 10-11. Plaintiff, however, does not adequately explain how this difference materially impacts the Court's analysis. Plaintiff also asserts that Dr. Major's testimony can overcome the super-presumption in favor of Defendants. The argument as to Dr. Major is addressed below.

Plaintiff's primary argument relies mainly on *McDarby v. Merck & Co., Inc.*, 401 N.J. Super. 10 (App. Div. 2008), a products liability action concerning the prescription drug Vioxx. The *McDarby* court recognized an exception to the presumption where a drug manufacturer has engaged in "economically-driven manipulation of the post-market regulatory process," because the pre-market approval process the FDA engages in is far more stringent than their oversight role after a drug has entered the market. *Id.* at 63-64.

At the outset, in setting forth the economically-driven manipulation test, *McDarby* broke from the New Jersey Supreme Court's two instances to overcome the statutory presumption: deliberate concealment or nondisclosure of after-acquired knowledge of harmful effects. *Perez*, 161 N.J. at 25 (1999). Plaintiff fails to cite to a Supreme Court of New Jersey decision that has adopted the *McDarby* variation.[6] Thus, it is not clear that the economically-driven manipulation exception applies.

Yet, assuming that the economically-driven manipulation standard applies, there is no genuine issue of material fact to support such a finding here. To the contrary, Biogen was attempting to develop two different assays to detect the JC Virus. Biogen also employed an

[6] The New Jersey Supreme Court acknowledged in *Kendall v. Hoffman-La Roche, Inc.*, that lower courts have "suggest[ed] that circumstances less egregious than deliberate concealment could overcome the presumption," citing to *McDarby*. 209 N.J. 173, 195 & n.6 (2017). However, the court did "not resolve that issue" in *Kendall*. *Id.*

advisory board and sponsored two clinical trials, STRATIFY-1 and STRATIFY-2. In addition, Biogen publically disclosed the additional cases of PML. Finally, in 2010, Biogen sought FDA approval (by way of CDER and CDRH) for both a label change and approval of its assay, but the FDA rejected both requests.

As a result, the facts in *McDarby* are easily distinguishable. There, the FDA was the motivating force behind the label changes to Vioxx. In fact, an article even characterized the FDA at having "'force[d] Merck, the manufacturer of Vioxx, to add a warning of the risks of heart attack and stroke to Vioxx's label.'" *McDarby*, 401 N.J. Super at 65 (citation omitted). The *McDarby* court also noted that Merck's marketing staff "engaged in strenuous efforts" to make sure that the results of one of their studies "were not communicated to prescribing physicians," and worse, that there was evidence Merck may have lied to doctors who asked them questions about the harmful effects of Vioxx. *Id.* at 68. Merck also downplayed adverse cardiovascular events and attributed differences between Vioxx and anther product, Naproxen, to a scientifically unsubstantiated property in Naproxen. *Id.* Plaintiff can point to no such evidence here to overcome the *McDarby* exception.

Besides their separate *Daubert* motion, Defendants raise several issues with the testimony of Dr. Major in their motion for summary judgment. Defendants argue that without a competent neurologist's testimony, Plaintiff cannot prove the label was inadequate or show proximate cause. Dr. Major is not a neurologist nor a medical doctor, and Plaintiff has proffered no other expert evidence. Plaintiff nevertheless argues that Dr. Major's testimony raises a "genuine issue of material fact" that precludes summary judgment. Opp. at 22-23.

As noted, New Jersey adheres to the learned intermediary rule. Thus, Plaintiff has to show

that the warning was inadequate as to the treating physician, rather than to Plaintiff.[7] The court in *Christison* addressed the same issue, finding that an expert had to testify as to the adequacy of the label because it is outside the ken of a juror's "own life experiences." *Christison*, 119 F.Supp. at 1340-1. When interpreting the NJPLA, other courts in this District have similarly stated that expert testimony is required as part of a failure to warn claim, and without it, the claims "must ultimately fail." *See, e.g., Jones v. Synthes USA Sales, LLC*, 2010 U.S. Dist. LEXIS 85744, at *32 (D.N.J., Aug. 19, 2010). In other words, expert testimony is required when "the subject matter is so esoteric that jurors of common judgment and experience are unable to make a determination without the benefit of the information and opinions possessed by a person with specialized knowledge." *Grobelny v. Baxter Healthcare Corp.*, 2008 U.S. Dist. LEXIS 41115, at *4-5 (D.N.J. May 22, 2008) (holding that an expert witness was required in a case about a "complex pharmaceutical compound"); *cf. Macri v. Ames McDonough Co.*, 211 N.J. Super. 636, 642 (App. Div. 1986) (holding that an expert witness was not required to testify about the adequacy of a warning for a household hammer).

Under the NJPLA, in addition to proving the product was defective, a plaintiff must also show that "the defect was the proximate cause of the plaintiff's damages." *London v. Lederle Laboratories, Div. of American Cyanamid Co.*, 290 N.J. Super. 318, 326-7 (App. Div. 1996); N.J.S.A. 2A:58C-2. "Where the failure-to-warn case involves a prescription drug, the issue is whether the warning should have been given to the prescribing physician," and the "plaintiff must prove that the warning's absence was the proximate cause of the harm." *Id.* (citing *Coffman v. Keene Corp.*, 133 N.J. 581, 593-4 (1993)); *see also Perez*, 161 N.J. at 25-30.

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[7] As also noted, however, Plaintiff was directly advised of, and acknowledged, the risk of Tysabri through the TOUCH program. Defendants' SOMF at ¶15.

Thus, pursuant to New Jersey law, in a case involving the adequacy of a prescription medication's label and warnings, expert testimony is necessary for Plaintiff to prove his case. The issue here is whether Plaintiff's proffered expert, Dr. Major, can fulfill this requirement. Plaintiff claims that Dr. Major is qualified to testify as to the adequacy of the warnings, *see* Opp. at 17, 20, but then later states that Dr. Major could opine on issues "directly relevant" to the adequacy of the label itself, *id.* at 20. However, testimony on issues "relevant" to the adequacy of the label is not the same as testifying to the adequacy of the warning itself. It appears that Plaintiff's argument is that Dr. Major will testify that Biogen could have developed the JC Virus antibody assay earlier, resulting in Plaintiff being tested for JC Virus antibodies before he developed PML. This testimony, according to Plaintiff, bears not only on the adequacy of the label but also proximate cause. Opp. at 20-21. In other words, Dr. Major's testimony is that Biogen could have developed the JC Virus antibody assay earlier, not that the label was inadequate when Plaintiff was receiving Tysabri infusions. *Id.*

Yet, Dr. Major admitted that he has never prescribed medication to a patient; he is not a medical doctor. *See* Ex. 12 to Marino Cert. at 142:20-21. Nor has he "counseled patients with respect to the risks and benefits of a particular MS medication." *Id.* at 143:24-25, 144:1-3. Dr. Major also acknowledged, "I am not familiar with the requirements for labeling for prescription drugs" as far as the use of assays. *See id.* at 212:24-25, 213:1. He also said that he did not know the relevant requirements "to approve or clear an assay to be used with the prescription of a drug," and that he was not an expert in MS as compared to "neurologists who see and treat patients." *Id.* at 120:22-25, 121:2, 142:14-17. In fact, Dr. Major declared that he was "not going to comment on the labeling" of Tysabri. *Id.* at 466:23-24.

By contrast, one of Plaintiff's prescribing physicians, Dr. Citak, testified that he was aware

of the PML risk in prescribing Tysabri and that, as a result, he was "more conservative" in prescribing the drug than before it was taken off the market. *See* Ex. 10 to Marino Cert at 85:12-23. Dr. Citak also discussed the risk of PML with Plaintiff before treating Plaintiff with Tysabri. *Id.* at 84:22-25, 85:1-6. Dr. Zabad, another prescribing physician, said that she understood that there is a risk of PML with Tysabri, and that "[i]t is something that we discuss with the patient all the time." *See* Ex. 11 to Marino Cert. at 51:24, 52:1-3. Dr. Zabad also explained: "[I]f I feel it's a reasonable option and it's within the prescription evidence, I will give [the patient] the choice." *Id.* at 66:9-11. Neither Dr. Citak nor Dr. Zabad stated that they would have made a different prescribing decision for Plaintiff had the JC Virus assay been available to them.[8] But Dr. Citak stated that he would have ordered a test. *See* Ex. 10 to Marino Cert. at 138:10-16, 146:23-25, 147:1-17.

The Court agrees with the conclusions reached by the *Gentile* and *Christison* courts concerning Dr. Major's proposed testimony and proximate cause. New Jersey law does not lead to a different result. Because Dr. Major is not a neurologist who treats MS, he is not qualified to opine as to the adequacy of the warning of the Tysabri label at any point in time. Dr. Major also frankly admits that he is not familiar with the labeling requirements or regulations for prescription medication. In contrast, Plaintiff's prescribing physicians explain that they knew the risks of prescribing Tysabri to Plaintiff, and, after discussing the risk directly with Plaintiff and obtaining his informed consent, they made the decision to administer Tysabri. As to Plaintiff's theory that Dr. Major will establish that Biogen could have developed its JC Virus antibody assay earlier, Plaintiff fails to support this theory with any controlling or persuasive authority. In sum, there is

[8] Dr. Zabad did test Plaintiff for "JC V[irus] DNA" three times in 2009; all of the tests were negative. Defendants' SOMF at ¶74.

not genuine issue of material fact that precludes summary judgment. Defendants are entitled to summary judgment because Plaintiff does not have the necessary expert testimony to challenge the adequacy of the Tysabri label or create a genuine issue as to probable cause.

c. Preemption

Defendants further argue that Plaintiff's NJPLA claim is preempted by federal law and that Elan is entitled to judgment as a matter of law because it could not effect changes to Tysabri's label. The Court agrees.

The Supremacy Clause of the Constitution provides that federal law "shall be the supreme Law of the Land." U.S. Const. art. VI, cl. 2. States are free to legislate as they see fit, "subject only to limitations imposed by the Supremacy Clause." *Tafflin v. Levitt*, 492 U.S. 455, 458 (1990). Federal law "preempts" state law in three situations: "(1) when a federal statute includes 'an express provision for preemption'; (2) '[w]hen Congress intends federal law to "occupy the field" in an area of law; and (3) when a state and federal statue are in conflict." *In re Foxomax (Alendronate Sodium) Products Liability Litigation (No. II)*, 751 F.3d 150, 158-159 (internal citations omitted). The third scenario, "conflict preemption," includes two types: impossibility preemption and obstacle preemption. *Id.* at 159. Impossibility preemption occurs when it is not possible to comply with both federal and state law. *Id.* Here, Defendants argue conflict preemption under the impossibility theory.

Drug manufacturers must seek FDA approval "to market a new drug," showing that "it is safe and effective and that the proposed label is accurate and adequate." *PLIVA, Inc. v. Mensing*, 564 U.S. 604, 612 (2011). Not only must a manufacturer use the label approved by the FDA, but "[g]enerally speaking, a manufacturer may only change a drug label after the FDA approves a supplemental application." *Wyeth v. Levine*, 555 U.S. 555, 568 (2009). However, FDA

regulations allow manufacturers to change the labels without FDA approval under the "Changes Being Effected" ("CBE") exception. *Id.* at 614 (citing 21 C.F.R. §314.70(c)(6)(iii)(A)). The exception allows a manufacturer to "add or strengthen a contraindication, warning, [or] precaution" without pre-approval from the FDA. *Id.* Nevertheless, if the manufacturer can show clear evidence that the FDA would not have approved the labeling change, the CBE exception does not apply. *See Wyeth*, 555 U.S. at 571.

Here, the Court agrees with the decisions in *Gentile*, *Christison*, and *Amos*: clear evidence of impossibility exists. There is clear evidence that FDA would not have approved an earlier change to the Tysabri label or have earlier approved the JC Virus antibody assay. In September 2010, Biogen proposed adding information to the Tysabri label about the use of the JC Virus antibody assay, including recommending screening patients before starting infusions. *See* Defendants' SOMF at ¶132-33. The FDA rejected that proposal because the underlying data was insufficient. *Id.* In November 2010, Biogen proposed making their JC Virus antibody assay "available to Tysabri prescribers," which the FDA again rejected because the usefulness of the test "had not been established." *Id.* at ¶¶134-35.

Plaintiff argues that the United States Supreme Court severely limited the application of federal preemption in *Wyeth v. Levine*, 555 U.S. 555 (2009). However, given the subsequent decisions in *Mensing*, 564 U.S. at 618; *Mutual Pharmaceutical Co., Inc. v. Bartlett*, 570 U.S. 472, 486-87 (2013); and *In re Fosomax*, 751 F.3d at 164-65, the Court disagrees. Plaintiff argues that the standard of proof for showing that the FDA would not have approved a change, per *Wyeth*, is very high, citing *Aaron v. Wyeth*, 2010 WL 653984 (W.D. Pa. Feb. 19, 2010); *Reckis v. Johnson & Johnson*, 471 Mass. 272 (2015); and *Forst v. SmithKline Beecham Corp.*, 639 F.Supp.2d 948 (E.D. Wis. 2009). *See* Opp. at 33. However, as Plaintiff admits, Opp. at 35, all three have different

"fact patterns" than the one at bar and none are from this jurisdiction.

"Clear evidence" is necessary to rebut the CBE exception, meaning that the drug manufacturer must present clear evidence that the FDA would have rejected the manufacturer's proposed changes to the label. *See Wyeth*, 555 U.S. at 571. Plaintiff argues that if Defendants had pressed their position in the September 2010 meeting with the FDA, something "might have" been added to the label (although Plaintiff does not indicate what that "something" might have been or how it would have changed the outcome here). Opp. at 40. Not only is this not the appropriate standard, it is clear from the record that the FDA would not have permitted a label change. In September 2010, Biogen disclosed all pertinent information to the FDA (including the number of PML cases), but the FDA nevertheless affirmatively stated that the label could not be amended. The FDA determined that the sample size was too small and inconclusive to warrant a label change. Defendants' SOMF at ¶129.

Plaintiff also relies on *In re Fosomax*, 852 F.3d 286 (3d Cir. 2017), arguing that the "clear evidence" standard is always a question of fact for the jury. Opp. at 36-37. However, the Third Circuit in *Fosomax*, while acknowledging that issue would normally be one for the jury, also stated that "[w]hen there is no issue of genuine material fact—that is, when no reasonably jury applying the clear evidence standard of proof could conclude that the FDA would have approved a label change—the manufacturer will be entitled to judgment as a matter of law." *In re Fosomax*, 852 F.3d at 282. In fact, the *Amos* court considered the Third Circuit's decision in *Fosomax* and still granted summary judgment for Defendants. *See Amos*, 249 F.Supp. 3d at 699. Indeed, the Third Circuit in *Fosomax* found that the state law claims were preempted as a matter of law. 852 F.3d at 165.[9]

[9] Plaintiff further attempts to distinguish the *Gentile* and *Amos* because, in those cases, the

Plaintiff has also failed to show that Elan had the power to change the label. Opp. at 43-44. Plaintiff merely cites to several cases that are not on point. *Id.* Because Elan was not the United States license holder, it could not effect change to the label. Plaintiff has shown no facts or law to the contrary. Thus, summary judgment is also appropriate for Elan on this ground.

IV. Conclusion

For the reasons stated above, Defendants' motion for summary judgment is **GRANTED** and their *Daubert* motion is **DENIED** as moot. To be clear, both Defendants are entitled to summary judgment for the following, distinct reasons: (1) the Tysabri warnings were adequate as a matter of law; (2) Plaintiff does not have the necessary expert evidence to challenge the adequacy of the warnings (which, relatedly, also means that Plaintiff cannot establish proximate cause); and (3) federal preemption. Elan is also entitled to summary judgment for the separate reason that it is not the holder of the necessary license. An appropriate Order accompanies this Opinion.

Dated: April 25, 2018

John Michael Vazquez, U.S.D.J.

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patients were diagnosed with PML before Defendants approached the FDA in 2010 to discuss a labeling change. *See* Opp at 39-40. The Court disagrees. Here, it is uncontroverted that Defendants approached the FDA before Plaintiff was diagnosed, and the FDA nevertheless rejected Biogen's proposal to change the label. Soon after the FDA rejected the proposal, Plaintiff was diagnosed with PML. The FDA's actual rejection is clear evidence; indeed, it is difficult to conceive of stronger evidence in Defendants' favor.